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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/856,274	05/18/2001	Sulayman D. Dib-Hajj	2009399-0015	5193

24280 7590 05/14/2010

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EXAMINER	
PAK, MICHAEL D	
ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
05/14/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	09/856,274	DIB-HAJJ ET AL.	
	Examiner	Art Unit	
	Michael Pak	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 February 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *20,22-31,35,36 and 40-44* is/are pending in the application.

4a) Of the above claim(s) *32-33, 37-39* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *20,22-31,35,36 and 40-44* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *2-3-10*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

1. Claims 20, 22-31, 35-36, and 40-44 are examined below. Claims 32-33 and 37-39 are withdrawn. Claims 1-19 and 34 are cancelled.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 20, 22-31, 35-36 and 40-44 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The first paragraph of § 112 requires that the patent specification enable "those skilled in the art how to make and use the full scope of the claimed invention without `undue experimentation.'" Genentech, Inc. v. Novo Nordisk AIS, 108 F.3d 1361, 1365, 42 USPQ2d 1001, 1004 (Fed. Cir. 1997) (quoting In re Wright, 999 F.2d 1557, 1561, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)); see also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). ("[T]he scope of the claims must bear a reasonable correlation to the scope of enablement provided by the specification to persons of ordinary skill in the art."). Whether making and using the invention would have required

undue experimentation, and thus whether the disclosure is enabling is a legal conclusion based upon several underlying factual inquiries. See In re Wands, 858 F.2d 731, 735, 736-37, 8 USPQ2d 1400, 1402, 1404 (Fed. Cir. 1988). As set forth in Wands, the factors to be considered in determining whether a claimed invention is enabled throughout its scope without undue experimentation include the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art, and the breadth of the claims.

Likewise, in Amgen Inc. v. Chugai Pharm. Co., 927 F.2d 1200, 18 USPQ2d 1016 (Fed. Cir. 1991), the court affirmed the holding of invalidity of claims to analogs of the EPO gene under § 112 for lack of enablement where applicants had claimed every possible analog of the EPO gene but had disclosed only how to make EPO and a very few analogs. "[D]espite extensive statements in the specification concerning all analogs of the EPO gene that can be made, there is little enabling disclosure of the particular analogs and how to make them .... There may be many other genetic sequences that code for EPO-type products. Amgen has told how to make and use only a few of them and is therefore not entitled to claim all of them." Id., 927 F.2d at 1213-14, 18 USPQ2d at 1027.

Claims encompass method of treatment of treating neuropathic pain in a human suffering from neuropathic pain by administering to a human GDNF in amount to alleviate the neuropathic pain where the GDNF alters tetrodotoxin-resistant sodium ion

current in neuronal cells. However, one skilled in the art was not aware at the time of the invention how to treat all neuropathic pain in a human suffering from neuropathic pain by administering to a human GDNF in amount to alleviate neuropathic pain where the GDNF alters tetrodotoxin-resistant sodium ion current in neuronal cells. The nexus between pain treatment and GDNF is not directly established with animal model of pain by administering GDNF but only show GDNF effect on sodium channels and thus its effect on pain by inference. The amount of direction provided in the specification is limited to prophetic examples. No treatment of neuropathic pain in human is provided in the examples. One skilled in the art would require empirical experimentation in order to determine the treatment of clinical conditions to treat neuropathic pain. The state of the art at the time of the invention was was limited to nerve growth factor (NGF) as the primary neurotrophic factor whose relationship with neuropathic pain was known (Diamond et al. US 6,630,478). However, Diamond et al. teaches that NGF enhances neuropathic pain (page 4; reciting Ramer et al. reference). Thus, the state of the art at the time of the invention was an unpredictable art because no information regarding GDNF treatment of neuropathic pain was known and the best known neurotrophic factor caused neuropathic pain. The post filing date reference, Boucher et al. (Science, 2000) is the first to teach the administration of GDNF for treatment of neurotrophic pain in animal models. Boucher et al. provided direct testing of neuropathic pain behavior with electrophysiological recording when GDNF was administerd. The working example on the other hand do not provide testing of neuropathic pain behavior and direct measurement of electrophysiological recording to correlate neuropathic pain with

GDNF. The working example provided in the specification is not sufficient for one of skilled in the art to treat neuropathic pain at the time of the invention. It would require empirical experimentation to determine a method of treating neuropathic pain with GDNF. Furthermore, claims encompass a large genus of neuropathic pain, whereas the specification does not teach how to treat all forms of neuropathic pain. Post filing date references are limited to peripheral neuropathic pain in the sensory neurons using specific pain inducing model (Boucher et al.). Post filing date references teach conflicting evidence regarding the role of nociceptors in pain (Boucher et al., page 127) leading one skilled in the art to the unpredictable nature of treating neuropathic pain. In view of the extent and the unpredictability of the experimentation required to practice the invention as claimed, one skilled in the art could not make the invention without undue experimentation. Therefore, based on the above Wands analysis, a preponderance of the evidence supports a conclusion that one skilled in the art would not have been enabled to make and use the claimed invention without undue experimentation.

Applicants argue that art at the time of invention (Matzner et al.) include clear relationship between abnormal firing in injured afferent and parathesias and pain that often accompany nerve injury i.e. neuropathic pain. However, it should be noted that Matzner et al. disclose specifically peripheral sciatic nerve neuroma model and electrophysiological measurement of channels but does not create a nexus between all neuropathy and pain and effect of GDNF.

Applicants argue that '067 patent teach the channels and peripheral nerve injury and pain. However, the '067 patent does not teach it for all neuropathy but only peripheral neuropathy model. Furthermore, specific example is not provided for effect of GDNF on pain in any model.

Applicants argue that example 8 of the specification teach the effect of GDNF on sodium channel expression. However, no nexus is established between GDNF and pain. The example infers the relationship between GDNF to pain via sodium channel expression but does not directly teach the GDNF effect on pain models.

3. No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

4. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Pak whose telephone number is 571-272-0879. The examiner can normally be reached from 8:30 to 2:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael Pak/
Primary Examiner, Art Unit 1646